Original Article

Comparison of prophylactic use of ketamine, tramadol, and dexmedetomidine for prevention of shivering after spinal anesthesia

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Abstract

Background and Aims: Shivering after spinal anesthesia is a common complication and can occur in as many as 40%–70% of patients after regional anesthesia. This shivering, apart from its physiological and hemodynamic effects, has been described as even worse than surgical pain. The aim of the study was to evaluate and compare the effectiveness of prophylactic use of intravenous (IV) ketamine, dexmedetomidine, and tramadol for prevention of shivering after spinal anesthesia.

Material and Methods: Two hundred American Society of Anesthesiologists physical status I and II patients subjected to spinal anesthesia were included in the study. The subjects were randomly divided into four groups to receive either ketamine 0.5 mg/kg IV or tramadol 0.5 mg/kg IV or dexmedetomidine 0.5 microgm/kg IV or 10 mL of 0.9% normal saline (NS). All the drugs/NS were administered as IV infusion over 10 min immediately before giving spinal anesthesia. Temperature (core and surface), heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure, peripheral oxygen saturation were assessed before giving the intrathecal injection and thereafter at 5 min intervals. Important side effects related to study drugs were also noted.

Results: Shivering after spinal anesthesia was comparatively better controlled in group receiving dexmedetomidine as compared to other groups ($P = 0.022$). However, the use of dexmedetomidine was associated with significant hypotension which responded to single dose of mephentermine (3 mg IV). Dexmedetomidine is a better agent for prevention of shivering after spinal anesthesia as compared to ketamine and tramadol. It also provides adequate sedation and improves the surgical conditions.

Conclusion: Dexmedetomidine is effective and comparably better than tramadol or ketamine in preventing shivering after spinal anesthesia. Dexmedetomidine also provides sedation without respiratory depression and favorable surgical conditions. However, with its use a fall in blood pressure and heart rate is anticipated.

Keywords: Dexmedetomidine, shivering, spinal anesthesia

Introduction

Shivering is one of the consequences of perioperative hypothermia. It occurs frequently after anesthesia, and the mechanisms leading to shivering remain poorly understood.[1] Postanesthetic shivering is a common complication of anesthesia and may affect up to 5%–65% of patients during general anesthesia and up to 33% of patients during epidural regional anesthesia.[2] Apart from discomfort, postanaesthetic shivering may be associated with increased oxygen consumption, carbon dioxide output and minute ventilation,[3] catecholamine release, increased cardiac output, tachycardia and hypertension, and increased intraocular pressure.[4] Shivering may also decrease mixed venous oxygen saturation[5] and may also interfere with monitoring.[6,7]

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Shivering is uncomfortable for the patients and has been reported worse than the surgical pain.[1] Shivering may aggravate postoperative pain by stretching the surgical incision. The increase in metabolic requirement may predispose to difficulties in patients with existing intrapulmonary shunts, patients with fixed cardiac output states, or those with limited respiratory reserves.

Both, the prevention of shivering and the treatment of established shivering should be attempted in the perioperative period. Anesthesiologists may therefore wish to prevent shivering by using pharmacological strategies in selected surgical patients.[8]

Material and Methods

The study was conducted at a tertiary care hospital and approval from the institutional ethical committee was obtained. A written informed consent was taken from all the patients. Patients in the American Society of Anaesthesiologists (ASA) physical status Class I or II, aged 21–60 years and scheduled for lower abdominal or lower limb surgeries under spinal anesthesia were included in the study. Patients with thyroid or neuromuscular diseases, pregnant females, patients on narcotics/sedatives, or with history of febrile illness, patients who required blood transfusion during surgery, or patients with an initial body (core) temperature >38.0°C or <36.0°C were excluded from the study.

The study was carried out in 200 patients and the participants were randomized into four groups of 50 patients each. Randomization was carried out using computer generated random numbers and sealed envelope technique, such that:

a. Group K - patients receiving ketamine 0.5 mg/kg intravenous (IV) diluted in 10 mL of normal saline (NS) given as IV infusion over 10 min[9-12]
b. Group T - patients receiving tramadol 0.5 mg/kg diluted in 10 mL of NS given as IV infusion over 10 min
c. Group D - patients receiving dexmedetomidine 0.5 mcg/kg diluted in 10 mL of NS given as IV infusion over 10 min
d. Group C - patients receiving 10 mL of NS given as IV infusion over 10 min.

The infusion was administered just before administering the spinal anesthesia.

The sample size was calculated using two independent sample proportions by doing a pilot study for Group D and Group C for the occurrence of shivering. Analysis of data obtained from this pilot study revealed 24% of patients in control group and 5% of patients in Group D had significant shivering (i.e., grade of shivering ≥3). With the power of the study aimed at 80%, and 95% confidence interval, the minimum sample size in each group was calculated as 50.

Preoperative preparations included nil per-oral for 6–8 h before the surgery. No premedication was given to the patients prior to the surgery. On arrival of the patient in the operating room, a peripheral IV access was obtained using an 18G venous cannula. All the ASA monitoring standards were followed including heart rate, electrocardiogram, noninvasive blood pressure, saturation of hemoglobin with oxygen (SpO_2), and temperature monitoring. Baseline reading of all the parameters was noted. Surface temperature was noted with temperature probe attached to one axilla of the patient, and the core temperature was noted using a nasopharyngeal temperature probe.

IV fluids were preheated to 37°C in a warmed cabinet and given without in-line warming. No other warming device was used. Lactated Ringer's solution warmed to 37°C was infused at 10 mL/kg/h over 30 min just before spinal anesthesia was administered. The infusion rate was thereafter reduced to 6 mL/kg/h till the end of surgery.

Study drug was coded and given as IV infusion over 10 min just before giving the neuraxial block by an anesthesiologist not involved in the management of the patient. Spinal anesthesia was instituted at L3–4 or L 4–5 interspace with patient in lateral position with 2.8 mL (14 mg) of bupivacaine (heavy) 0.5% using a 25G Quincke's spinal needle. Temperature (core and surface), heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure (MAP), peripheral oxygen saturation (SpO_2) and level of sensory block were assessed before intrathecal injection and thereafter at 5 min intervals. Sensory block was assessed every 5 min intervals till there was no change in the level of anesthesia. The ambient temperature was measured by a wall thermometer and was maintained at 24°C ± 1°C. All the patients were draped using a single layer of surgical drapes for the surgery.

The presence of shivering was observed and graded from 0 to 4 using a scale,[13] where 0 indicated no shivering and 4 indicated shivering all over the body. The degree of sedation was assessed according to Ramsay sedation score,[14] where a score of 1 indicated that the patient is anxious and agitated or restless or both, and a highest score of 6 indicated that the patient exhibits no response.

If the grade of shivering was 3 or 4 after 15 min from the administration of the prophylactic drug, rescue treatment in the form of injection pethidine 25 mg IV was administered. Side

effects such as hypotension, bradycardia, nausea, vomiting, sedation, and hallucinations were recorded.

Hypotension, defined as a decrease in MAP of more than 20% from the baseline, was treated by increasing the rate of IV fluid from 6 mL/kg/h to 10 mL/kg/h, and if required, with an IV incremental bolus dose of mephentermine 3 mg. Symptomatic bradycardia was managed with 0.6 mg of injection atropine given IV.

Statistical analysis

Statistical analysis was performed usiong the SPSS statistical package version 17.0 (Chicago, IL, USA). Continuous variables, including hemodynamic data and temperature values over time within the groups, were analyzed using analysis of variance (ANOVA) followed by Bonferroni's *post hoc* testing. Statistical comparisons among the groups were performed using two-way ANOVA, followed by unpaired *t*-tests with Bonferroni's correction.

Nominal or categorical data including the overall incidence of shivering between the four groups were analyzed and compared using the Chi-square test. Fisher's exact test was used when fewer than five patients were expected. Sedation score between the four groups were compared using the Kruskal–Willis test with further paired comparisons were performed using Mann–Whitney U-test. Values are given as mean ± standard deviation or median with minimum and maximum values. $P < 0.05$ was considered statistically significant.

Results

The mean age, gender, and the duration of surgery were comparable in all four groups and there was no statistically significant difference among the groups [Table 1].

While comparing the mean heart rate, there was a statistically significant difference among the groups throughout the duration of observation/surgery. For most of the observations, the highest and the lowest mean values were found in Group K and Group D, respectively. This difference in the mean heart rate can be explained by the physiological effects of these drugs (e.g., ketamine) on the cardiovascular system.

The four groups were comparable as regard the mean systolic blood pressures at 0 min and 5 min. This difference was, however, statistically significant at all other times. There was statistically significant difference among the groups, when they were compared on the variables of mean diastolic blood pressure and mean MAP. This difference is expected as ketamine has sympathomimetic effect on the cardiovascular system, whereas dexmedetomidine causes a decrease in heart rate and blood pressure.

There was statistically significant difference in the four groups throughout the duration of surgery, when the mean surface temperatures were compared. The surface temperatures showed progressively increasing trend in all four groups for most of the observations. The increase in mean surface temperature for the duration of observation was minimal in Group D [Figure 1]. The mean core temperatures in all four groups were comparable at all times except during 30–40 min observation periods [Figure 2].

The overall incidence of shivering in all four groups combined, was 40.5%. There was statistically significant difference among the four groups, when overall shivering grades were compared The incidence of shivering in Group K was 46%, Group T was 50%, Group C was 42% and Group D was 24%. Requirement of injection pethidine 25 mg IV for control of higher grades of shivering was 12% in Group K, 20% in Group T, 16% in Group C and 6% in Group D [Table 2 and Figure 3].

The overall sedation score, when compared among four groups was statistically significant. No patient had sedation scores of 5 and 6 on sedation scale in any group [Table 3].

No hallucinations or nausea/vomiting were observed in any of the study groups.

Patients who required treatment for symptomatic bradycardia in the form of injection atropine 0.6 mg IV were 4% in

Table 1: Comparison of patient demographics

Patient data	Group K	Group T	Group C	Group D	*P*
Age (years)	40.4±12.6	37.6±12.8	39.0±12.8	40.7±12.0	0.58
Gender (male/female)	40/10	34/16	38/12	37/13	0.612
Duration of surgery (min)	67.2±9.3	60.8±15.0	63.8±15.3	63.6±14.7	0.149

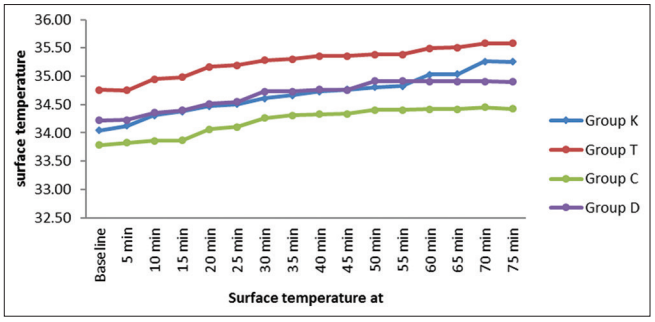

Figure 1: Comparison of mean surface temperatures (°C)

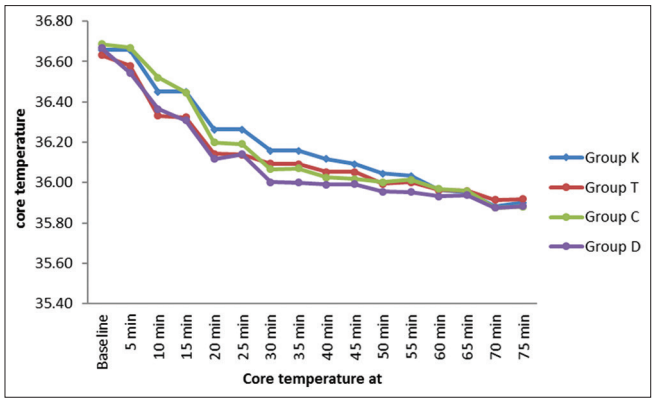

Figure 2: Comparison of mean core temperatures (°C)

Table 2: Comparison of grade of shivering

Group	Grade of shivering					Total	*P*
	0	1	2	3	4		
Group K	27	7	10	2	4	50	0.022
Group T	25	6	9	8	2	50	
Group C	29	7	6	2	6	50	
Group D	38	7	2	2	1	50	
Total	119	27	27	14	13	200	

Table 3: Comparison of sedation scores

Group	Sedation score					Total	*P*
	0	1	2	3	4		
Group K	0	6	30	13	1	50	<0.001
Group T	1	8	38	3	0	50	
Group C	1	10	38	1	0	50	
Group D	0	2	24	19	5	50	
Total	2	26	130	36	6	200	

Group K, 12% in Group T, 18% in Group C, and 10% in Group D.

Discussion

Various hypotheses have been proposed to explain the shivering after spinal anesthesia. Neuraxial anesthesia–induced inhibition of thermoregulatory mechanism leading to perioperative hypothermia is the primary cause. Perioperative shivering hence occurs as a thermoregulatory response to hypothermia. However, in the postoperative period, shivering may occur even with normothermia, which suggests that mechanisms other than heat loss and subsequent decrease in core temperature may lead to shivering. These mechanisms may be sympathetic over-activity, uninhibited spinal reflexes, postoperative pain, adrenal suppression and respiratory alkalosis. The patient recovery in the postoperative period may suffer because of shivering. Shivering by itself may aggravate postoperative pain, by stretching the surgical incision.[15,16]

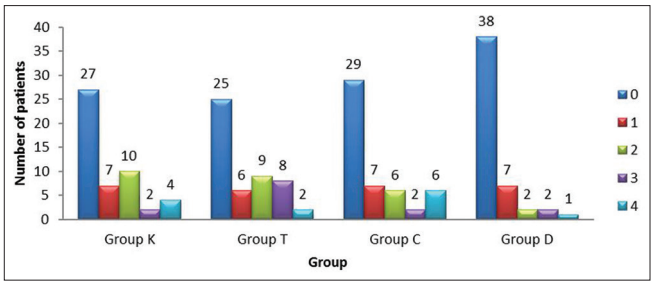

Figure 3: Comparison of grade of shivering

Among the various methods available for control of shivering, pharmacological methods using drugs such as pethidine, clonidine, tramadol, doxapram, katenserin, nefopam, etc., are cost-effective, simple, and easy to implement.[15]

Pharmacological agents such as ketamine and tramadol have been in use since long as agents for prevention and treatment of postanaesthetic shivering, however, dexmedetomidine's role in prevention of shivering has not been studied much. It has been used primarily as an analgesic and sedating agent. Ketamine causes sympathetic stimulation and vasoconstriction in patients at risk of hypothermia. Ketamine may control shivering by nonshivering thermogenesis either by its effects on the hypothalamus, or by the α-adrenergic effect of norepinephrine.

Tramadol is an opioid analgesic with its actions preferably mediated via μ receptor with minimal effect on κ and δ receptors. However, it has may have adverse effects in the form of nausea, vomiting, and dizziness which may cause further discomfort to the patient.[15,17,18]

The anti-shivering effects of dexmedetomidine are mediated by binding to α2-receptors that mediate vasoconstriction and the anti-shivering effect. In addition, it also has hypothalamic thermoregulatory effects. Dexmedetomidine reduces the vasoconstriction and shivering thresholds without altering the sweating threshold, suggesting its action on the central thermoregulatory system rather than peripheral actions. Thus dexmedetomidine may promote hypothermia and still be an effective treatment for postspinal shivering.[19]

The sedation provided by dexmedetomidine, without any nausea and vomiting, is beneficial for the patient as it provides comfort to the patient, maintains cardio-respiratory stability, provides improved surgical conditions and also provides amnesia during surgery.[20]

There was less shivering in Group D, despite a significant fall in core body temperature as compared to other groups. This might be due to higher sedative effects of dexmedetomidine, or it is possible that there are some other mechanisms responsible for anti-shivering properties of dexmedetomidine. The changes

in surface temperatures, apart from fall in core temperatures may also contribute to shivering.

The percentage of patients requiring treatment of in the form increasing the rate of IV fluids from 6 mL/kg/h to 10 mL/kg/h, and injection mephentermine were 50% in Group K, 56% in Group T, 50% in Group C, and 96% in Group D. The difference among the groups was statistically significant. However, the fall in MAP in Group D stabilized after a single dose of mephentermine in most cases, and subsequent doses were not required. The fall in MAP requiring pharmacological treatment may be because a higher dose of bupivacaine (heavy) of 2.8 mL was used for all the surgeries. This fall may be less, or may be absent if a lower dose of bupivacaine is used.

The results of the study are comparable to the results of the study done by Bozgeyik *et al.* where the authors have concluded that preemptive tramadol and dexmedetomidine are effective in preventing shivering after spinal anesthesia. Dexmedetomidine also provided sedation which is sufficient to prevent the anxiety without any adverse effects.[21] Usta *et al.* reported effective prevention of shivering and adequate sedation with the use of dexmedetomidine infusion in patients during spinal anesthesia.[22]

Prophylaxis of postoperative shivering with simple pharmacological interventions is possible and is clinically effective; however, prophylaxis may be useful in certain specific patient population like the patients with compromised cardiac supply. In these patients it may be worthwhile to give an antishivering drug prophylactically, and dexmedetomidine may be a good choice in these patients, because in addition to its antishivering effect, it has favorable effect on cardiac outcome and provides adequate sedation.

Conclusion

From the findings of our study, it can be concluded that dexmedetomidine is effective and comparably better than tramadol or ketamine in preventing shivering after spinal anesthesia. Apart from preventing shivering, dexmedetomidine offers other advantages in the form of sedation without any respiratory depression. However, with its use a watch should be kept on the fall hemodynamic parameters.

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Conflicts of interest
There are no conflicts of interest.

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